NUCLEIC ACID MOLECULES ENCODING GLUTX AND USES THEREOF

Background of the Invention

A number of mammalian glucose (hexose) transporters (GLUTs) have been identified. High affinity GLUTs are found in nearly every tissue. A low affinity GLUT (GLUT-2) is expressed in tissues which are associated with high glucose flux (*e.g.*, intestine, kidney, and liver). It is thought that the level of expression of high affinity GLUTs influences the rate of glucose uptake. It is also thought that the expression of various GLUTs is regulated by glucose and various hormones (Thorens, *Am. J. Physiol.* 270 (Gastrointest. Liver Physiol. 33:G541-G553, 1996). Human GLUT-1 is described by Mucckler et al. (*Science* 229:941, 1985). Human GLUT-2 is described by Fukumoto et al. (*Proc. Nat'l Acad. Sci. USA* 264:776, 1989). Human GLUT-3 is described by Keller et al. (*J. Biol. Chem.* 264:18884, 1989). Human GLUT-4 is described by Fukumoto et al. (*J. Biol. Chem.* 264:7776, 19 89). Human GLUT-5 is described by Kayano et al. (*Nature* 377:151, 1995).

Summary of the Invention

The invention described herein relates to the discovery and characterization of a cDNA encoding GLUTX, a human glucose transporter protein. The nucleotide sequence of a cDNA encoding GLUTX is shown in Fig. 1. The deduced amino acid sequence of GLUTX is shown in Fig. 2. GLUTX is predicted to include 12 transmembrane domains. The first transmembrane domain extends from about amino acid 52 (intracellular end) to about amino acid 71 (extracellular end). The second transmembrane domain extends from about

amino acid 108 (extracellular end) to about amino acid 128 (intracellular end). The third transmembrane domain extends from about amino acid 141 (intracellular end) to about amino acid 159 (extracellular end). The fourth transmembrane domain extends from about amino acid 166 (extracellular end) to about amino acid 189 (intracellular end). The fifth transmembrane domain extends from about amino acid 204 (intracellular end) to about amino acid 221 (extracellular end). The sixth transmembrane domain extends from about amino acid 233 (extracellular end) to about amino acid 252 (intracellular end). The seventh transmembrane domain extends from about amino acid 317 (intracellular end) to about amino acid 338 (extracellular end). The eighth transmembrane domain extends from about amino acid 355 (extracellular end) to about amino acid 375 (intracellular end). The ninth transmembrane domain extends from about amino acid 383 (intracellular end) to about amino acid 404 (extracellular end). The tenth transmembrane domain extends from about amino acid 413 (extracellular end) to about amino acid 437 (intracellular end). The eleventh transmembrane domain extends from about amino acid 449 (intracellular end) to about amino acid 472 (extracellular end). The twelfth transmembrane domain extends from about amino acid 481 (extracellular end) to about amino acid 499 (intracellular end). GLUTX nucleic acids and polypeptides, as well as molecules which increase or decrease expression or activity of GLUTX, are useful in the diagnosis and treatment of disorders associated with aberrant hexose transport.

GLUTX protein has some sequence similarity to a number of known glucose transporters (Fig. 3).

The invention features isolated nucleic acid molecules (*i.e.*, a nucleic acid molecule that is separated

from the 5′ and 3′ coding sequences with which it is immediately contiguous in the naturally occurring genome of an organism, also referred to as a recombinant nucleic acid molecule) that encodes a GLUTX polypeptide. Within the invention are polypeptides having the sequence of SEQ ID NO:2 or encoded by nucleic acid molecules having the sequence shown in SEQ ID NO:1. However, the invention is not limited to nucleic acid molecules and polypeptides that are identical to those SEQ ID Nos. For example, the invention includes nucleic acid molecules which encode splice variants, allelic variants or mutant forms of GLUTX as well as the proteins encoded by such nucleic acid molecules.

Also within the invention are nucleic acid molecules that hybridize under stringent conditions to a nucleic acid molecule having the sequence of SEQ ID NO:1. Such molecules include, for example, nucleic acid molecules encoding allelic variants of GLUTX or mutant forms of GLUTX. As described further below, molecules that are substantially identical to those of SEQ ID Nos. 1 and 2 are also encompassed by the invention.

The term "substantially pure" as used herein in reference to a given compound (*e.g.*, a GLUTX polypeptide) means that the compound is substantially free from other compounds, such as those in cellular material, viral material, or culture medium, with which the compound may have been associated (*e.g.*, in the course of production by recombinant DNA techniques or before purification from a natural biological source). When chemically synthesized, a compound of the invention is substantially pure when it is substantially free from the chemical compounds used in the process of its synthesis. Polypeptides or other compounds